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Atty. Dkt. No. NB 2004.02 (060925-0402)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: H. Michael SHEPARD et al.

Title: ENZYME CATALYZED
THERAPEUTIC AGENTS

Appl. No.: 09/782,721

Filing Date: 2/12/2001

Examiner: Crane, Lawrence E.

Art Unit: 1623

<p>CERTIFICATE OF MAILING</p> <p>I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as First Class Mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date below.</p> <p><u>Mary R. Zimmerman</u> (Printed Name)</p> <p><u>[Signature]</u> (Signature)</p> <p><u>April 14, 2006</u> (Date of Deposit)</p>
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SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT
UNDER 37 CFR §1.56

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
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Sir:

Submitted herewith on Form PTO/SB/08 is a listing of documents known to Applicants in order to comply with Applicants' duty of disclosure pursuant to 37 CFR §1.56.

A copy of each non-U.S. patent document and each non-patent document is being submitted to comply with the provisions of 37 CFR §1.97 and §1.98.

The submission of any document herewith, which is not a statutory bar, is not intended as an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicants do not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document which is determined to be a *prima facie* art reference against the claims of the present application.

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TIMING OF THE DISCLOSURE

The listed documents are being submitted in compliance with 37 CFR §1.97(c), before the mailing date of either a final action under 37 CFR §1.113, a notice of allowance under 37 CFR §1.311, or an action that otherwise closes prosecution in the application.

RELEVANCE OF EACH DOCUMENT

Applicants respectfully request that each listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

FEE

A check in the amount of \$180.00 is enclosed in accordance with 37 CFR §1.17(p) to cover the fee associated with an information disclosure statement under 37 CFR §1.97(c) in the amount of \$180.00.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 50-0872. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 50-0872.

Respectfully submitted,

Date

April 14, 2008

FOLEY & LARDNER LLP
Customer Number: 38706
Telephone: (650) 251-1129
Facsimile: (650) 856-3710

By

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Substitute for form 1449B/PTO				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: April 13, 2006 <i>(use as many sheets as necessary)</i>				Application Number	09/782,721
				Filing Date	2/12/2001
				First Named Inventor	H. Michael Shepard
				Group Art Unit	1623
				Examiner Name	Crane, Lawrence E.
Sheet	2	of	9	Attorney Docket Number	NB 2004.02 (060925-0402)

FOREIGN PATENT DOCUMENTS								
Examiner Initials*	Cite No. ¹	Foreign Patent Document			Name of Patentee or Applicant of Cited Documents	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Office ³	Number ⁴	Kind Code ⁵ (if known)				
	13	EP	0 095 294	A1	Beecham Group PLC	11-30-1983		
	14	EP	0 283 065	A1	Stichting REGA VZW	09-21-1988		
	15	RO	88451		Antibiotics Enperprise, Inc.	01-30-1986		✓
	16	WO	89/05817		Nucleic Acid Research Institute	06-29-1989		
	17	WO	92/20344		Glaxo Group Ltd.	11-26-1992		
	18	WO	95/01806		Kondratyev, A.	01-19-1995		
	19	WO	95/09865		Terrapin Technologies, Inc.	04-13-1995		
	20	WO	95/12678		Campaign Technology Limited	05-11-1995		
	21	WO	96/33168		Kumiai Chemical Industry Co. Ltd. et al.	10-24-1996		
	22	WO	99/06072		Boehringer Mannheim Corporation	02-11-1999		
	23	WO	99/08110		NewBiotics, Inc.	02-18-1999		
	24	WO	99/37753		NewBiotics, Inc.	07-29-1999		
	25	WO	00/33888		Coulter Pharmaceutical, Inc.	06-15-2000		

NON PATENT LITERATURE DOCUMENTS				
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	26	ASCHELE et al. "Immunohistochemical quantitation of thymidylate synthase expression in colorectal cancer metastases predicts for clinical outcome to fluorouracil-based chemotherapy" <i>J. Clin. Oncol.</i> (June 1999) 17(6):1760-1770		
	27	BAGSHAW, K.D. "Antibody-directed enzyme prodrug therapy: A review" <i>Drug Development Res.</i> (1995) 34(2):220-230		
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	29	BALZARINI et al. "The cytostatic activity of 5-(1-azidovinyl)-2'-deoxyuridine (AzVDU) against herpes simplex virus thymidine kinase gene-transfected FM3A cells is due to inhibition of thymidylate synthase and enhanced by UV light ($\lambda = 254$ nm) exposure" <i>FEBS Lett.</i> (1995) 373:41-44		

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	30	BALZARINI et al. "Mechanism of anti-HIV action of masked alaninyl d4T-MP derivatives" <i>PNAS USA</i> (July 1996) 93 :7295-7299	
	31	BARBATO et al. "Synthesis of bridged pyrimidine nucleosides and triazo [4, 3-c] pyrimidine nucleoside analogues" <i>Nucleosides & Nucleotides</i> (1989) 8 (4):515-528	
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	33	BATHE et al. "Increased thymidylate synthase gene expression in liver metastases from colorectal carcinoma: implications for chemotherapeutic options and survival" <i>Cancer J. Sci. Am.</i> (1999) 5 (1):34-40	
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	37	CATUCCI et al. "Development and significance of the HIV-1 reverse transcriptase M184V mutation during combination therapy with lamivudine, zidovudine, and protease inhibitors" <i>J. Acquir. Immune Defic. Syndr.</i> (1999) 21 :203-208	
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	39	CORDON-CARDO and PRIVES "At the crossroads of inflammation and tumorigenesis" <i>J. Exp. Med.</i> (November 15, 1999) 190 (10):1367-1370	
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	42	CURT "Cancer drug development: new targets for cancer treatment" <i>Oncologist</i> (1996) 1 (3):II-III	

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	43	CURTIN et al. "Mechanism of Cell Death following Thymidylate Synthase Inhibition: 2'-Deoxyuridine-5'-triphosphate Accumulation, DNA Damage, and Growth Inhibition following Exposure to CB3717 and Dipyridamole" <i>Cancer Res.</i> (May 1, 1991) 51 :2346-2352		
	44	DeCLERCQ et al. "Antiviral Activity of Novel Deoxyuridine Derivatives" <i>Current Chemotherapy: Proceedings of the International Congress of Chemotherapy</i> (September 18, 1978) 1:352-354		
	45	DeCLERCQ "Antiviral Activity Spectrum and Target of Action of Different Classes of Nucleoside Analogues" <i>Nucleosides & Nucleosides</i> (1994) 13(6&7) :1271-1295		
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	50	FARROW et al. "Synthesis and biological properties of novel phosphotriesters: A new approach to the introduction of biologically active nucleotides into cells" <i>J. Med. Chem.</i> (1990) 33(5) :1400-1406		
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	55	GREM "Biochemical modulation of fluorouracil by dipyridamole: preclinical and clinical experience" <i>Semin Oncol.</i> (April 1992) 19(2 Suppl 3):56-65	
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	61	HOWELL et al. "Comparison of the Synergistic Potentiation of Etoposide, Doxorubicin, and Vinblastine Cytotoxicity by Dipyridamole" <i>Cancer Res.</i> (June 15, 1989) 49:3178-3183	
	62	HU et al. "Determination of absorption characteristics of AG337, a novel thymidylate synthase inhibitor, using a perfused rat intestinal model" <i>J. Pharmaceutical Sciences</i> (July 1998) 87(7):886-890	
	63	HUSAIN et al. "Elevation of topoisomerase I messenger RNA, protein, and catalytic activity in human tumors: Demonstration of tumor-type specificity and implications for cancer chemotherapy" <i>Cancer Research</i> (January 15, 1994) 54:539-546	
	64	JACKMAN "Folate-based thymidylate synthase inhibitors as anticancer drugs" <i>Ann. Oncol.</i> (1995) 6(9):871-881	
	65	JOHNSTON et al. "Thymidylate synthase gene and protein expression correlate and are associated with response to 5-fluorouracil in human colorectal and gastric tumors" <i>Cancer Res.</i> (1995) 55:1407-1412	
	66	JONES and MANN "New methods of synthesis of β -aminoethylpyrazoles" <i>J. Am. Cancer Soc.</i> (1953) 75:4048-4052	

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	67	KOMAKI et al. "Difference in thymidylate synthetase activity in involved nodes compared with primary tumor in breast cancer patients" <i>Breast Cancer Res. Treat.</i> (1995) 35(2) :157-162		
	68	KRAJEWSKA et al. "Pyrimidine ribonucleoside phosphorylase activity VS 5- and/or 6-substituted uracil and uridine analogues, including conformational aspects" <i>Biochem. Pharmacol.</i> (1982) 31(6) :1097-1102		
	69	KRAUPP et al. "Membrane Transport of Nucleobases: Interaction with Inhibitors" <i>Gen. Pharmacol.</i> (1995) 26(6) :1185-1190		
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	72	LEHMAN et al. "Modulation of RTX cytotoxicity by thymidine and dipyridamole in vitro: implications for chemotherapy" <i>Cancer Chemother. Pharmacol.</i> (2000) 45 :142-148		
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	75	LENZ et al. "Thymidylate Synthase mRNA Level in Adenocarcinoma of the Stomach: A Predictor for Primary Tumor Response and Overall Survival" <i>J. Clin. Oncol.</i> (1995) 14(1) :176-182		
	76	LENZ et al. "p53 and thymidylate synthase expression in untreated stage II colon cancer: associations with recurrence, survival, and site" <i>Clinical Cancer Research</i> (May 1998) 4 :1227-1234		
	77	LEŠ et al. "Modeling of reaction steps relevant to deoxyuridylate (dUMP) enzymatic methylation and thymidylate synthase mechanism-based inhibition" <i>Journal of Biomolecular Structure & Dynamics</i> (1998) 15(4) :703-715		
	78	LEWIS et al. "Differential responses of human tumor cell lines to anti-p185HER2 monoclonal antibodies" <i>Cancer Immunol. Immunother.</i> (1993) 37(4) :255-263		

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	79	LIVINGSTON et al. "Studies with tetrahydrohomofolate and thymidylate synthetase from amethopterin-resistant mouse leukemia cells" <i>Biochem.</i> (1968) 7(8) :2814-2818		
	80	LOOK et al. "Increased thymidine kinase and thymidylate synthase activities in human epithelial ovarian carcinoma" <i>Anticancer Res.</i> (1997) 17 :2353-2356		
	81	MADEC et al. "Some characteristics of fetal and adult isoenzymes of thymidine kinase in human breast cancers" <i>Bull. Cancer</i> (1998) 75 :187-194		
	82	MADER et al. "Resistance to 5-fluorouracil" <i>Gen. Pharma.</i> (1998) 31(5) :661-666		
	83	MAHALINGAM et al. "Structural and kinetic analysis of drug resistant mutants of HIV-1 protease" <i>Eur. J. Biochem.</i> (1999) 263 :238-245		
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				Filing Date	2/12/2001
				First Named Inventor	H. Michael Shepard
				Group Art Unit	1623
				Examiner Name	Crane, Lawrence E.
Sheet	8	of	9	Attorney Docket Number	NB 2004.02 (060925-0402)

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	93	PARADISO et al. "Thymidilate synthase and p53 primary tumour expression as predictive factors for advanced colorectal cancer patients" <i>British J. of Cancer</i> (2000) 82(3) :560-567		
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